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(54) Title: OLIGOMERS FOR MODULATING RAS ONCOGENE

(57) Abstract

The present invention provides oligomers useful for modulation of expression of the human ras gene in both the normal and activated forms in which the oligomers are comprised of subunits, at least one of which is a protein nucleic acid subunit. Such oligomers can be used for diagnostics as well as for research purposes. Methods are also disclosed for modulating ras gene expression in cells and tissues using the oligomers provided, and for specific modulation of expression of the activated ras gene. Methods for diagnosis, detection and treatment of conditions arising from the activation of the H-ras and K-ras genes are also disclosed.

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OLIGOMERS FOR MODULATING RAS ONCOGENE

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation in part of U.S. Serial No. 08/032,752 filed March 17, 1993 which is a continuation-in-part of U.S. Serial No. 07/990,303 filed December 14, 1992 which is a continuation-in-part of U.S. Serial No. 007,996 filed January 21, 1993 which is a continuation-in-part of U.S. Serial No. 958,134 filed October 5, 1992 which is a continuation-in-part of U.S. Serial No. 715,196 filed June 14, 1991. These applications are assigned to the assignee of this invention. The entire disclosure of each is incorporated herein by reference.

FIELD OF THE INVENTION

This invention is directed to compounds that are not polynucleotides yet which bind in a complementary fashion to DNA and RNA strands. In particular, the invention concerns compounds wherein naturally-occurring nucleobases or other nucleobase-binding moieties are covalently bound to a polyamide backbone. This invention further provides methods for the inhibition of expression of the ras gene, a naturally occurring gene which occasionally converts to an activated form which has been implicated in tumor formation. This invention is also directed to the specific inhibition of expression of the activated form of the ras gene. This invention is further directed to the detection of both normal and activated forms of the ras gene in cells and tissues, and can form the basis for research reagents and kits both for

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research and diagnosis. Furthermore, this invention is directed to treatment of such conditions as arise from activation of the ras gene.

BACKGROUND OF THE INVENTION

5 Oligodeoxyribonucleotides (DNAs) as long as 100 base pairs (bp) are routinely synthesized by solid phase methods using commercially available, fully automatic synthesis machines. The chemical synthesis of oligoribonucleotides (RNAs), however, is far less routine.
10 Oligoribonucleotides are also much less stable than oligodeoxyribonucleotides, a fact which has contributed to the more prevalent use of oligodeoxyribonucleotides in medical and biological research directed to, for example, gene therapy or the regulation of transcription or
15 translation.

Genes function by transferring information to a messenger RNA (mRNA) molecule, a process referred to as transcription. The interaction of mRNA with the ribosomal complex directs the synthesis of a protein encoded within its
20 sequence. This synthetic process is known as translation and requires the presence of various co-factors and building blocks, the amino acids, and their transfer RNAs (tRNA), all of which are present in normal cells.

The initiation of transcription requires specific
25 recognition of a promoter DNA sequence by the RNA-synthesizing enzyme, RNA polymerase. In many cases in prokaryotic cells, and most likely in all cases in eukaryotic cells, this recognition is preceded by sequence-specific binding of protein transcription factors to the promoter.
30 Other proteins which bind to the promoter, but whose binding prohibits action of RNA polymerase, are known as repressors. Thus, gene activation is typically regulated positively by transcription factors and negatively by repressors.

Most conventional drugs function by interaction
35 with and modulation of one or more targeted endogenous proteins, e.g., enzymes. However, such drugs are typically

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not specific for targeted proteins but interact with other proteins as well. Thus, a relatively large dose of drug must be used to effectively modulate a targeted protein. Typical daily doses of drugs are from 10^{-5} - 10^{-1} millimoles per 5 kilogram of body weight or 10^{-3} - 10 millimoles for a 100 kilogram person. If this modulation could instead be effected by interaction with and inactivation of mRNA, a dramatic reduction in the necessary amount of drug could likely be achieved, along with a corresponding reduction in 10 adverse side effects. Further reductions could be achieved if such interaction could be rendered site-specific. Given that a functioning gene continually produces mRNA throughout the life of the cell, it would thus be even more advantageous if gene transcription could be arrested in its entirety.

15 Oligodeoxynucleotides offer such opportunities. For example, synthetic oligodeoxynucleotides could be used as antisense probes to block and eventually lead to the breakdown of mRNA. Thus, synthetic DNA could suppress translation *in vivo*. It also may be possible to modulate the 20 genome of an animal by, for example, triple helix formation using oligonucleotides or other DNA recognizing agents. However, there are a number of drawbacks associated with 25 triple helix formation. For example, it can only be used for homopurine sequences and it requires unphysiologically high ionic strength and low pH.

Furthermore, unmodified oligonucleotides are impractical both in the antisense approach and in the triple helix approach because they have short *in vivo* half-lives, and are difficult to prepare in more than milligram 30 quantities and, thus, are prohibitively costly. They are also poor penetrators of the cell membrane.

These problems have resulted in an extensive search for improvements and alternatives. For example, the problems arising in connection with double-stranded DNA (dsDNA) 35 recognition through triple helix formation have been diminished by a clever "switch back" chemical linking whereby a sequence of polypurine on one strand is recognized, and by

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"switching back", a homopurine sequence on the other strand can be recognized. Also, competent helix formation has been obtained by using artificial bases, thereby improving binding conditions with regard to ionic strength and pH.

5 In order to improve half life as well as membrane penetration, a large number of variations in polynucleotide backbones has been undertaken, although so far not with the desired results. These variations include the use of methylphosphonates, monothiophosphates, dithiophosphates, 10 phosphoramidates, phosphate esters, bridged phosphor-amidates, bridged phosphorothioates, bridged methylene-phosphonates, dephospho internucleotide analogs with siloxane bridges, carbonate bridges, carboxymethyl ester bridges, acetamide bridges, carbamate bridges, thioether, sulfoxy, 15 sulfono bridges, various "plastic" DNAs, α -anomeric bridges, and borane derivatives.

The great majority of these modifications has led to decreased stability for hybrids formed between the modified oligonucleotide and its complementary, native 20 oligonucleotide, as assayed by measuring T_m values. Consequently, it is generally understood in the art that backbone modifications destabilize such hybrids, i.e., result in lower T_m values, and should be kept to a minimum.

In WO 92/20702, moieties denominated peptide 25 nucleic acids (PNAs) are disclosed wherein ligands are linked to a polyamide backbone through aza nitrogen atoms. In U.S. Serial No. 08/054,363 filed April 26, 1993, peptide nucleic acids are disclosed in which their recognition moieties are linked to the polyamide backbone additionally through amido 30 and/or ureido tethers. PCT/EP 92/01219 filed May 22, 1992 also discloses protein nucleic acids.

These peptide nucleic acids are synthesized by adaptation of certain peptide synthesis procedures, either in solution or on a solid phase. The synthons used are certain 35 monomer amino acids or their activated derivatives, protected by standard groups. These oligonucleotide analogs also can

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be synthesized by using the corresponding diacids and diamines.

Peptide nucleic acid oligomers have been found to be superior to prior reagents in that they have significantly higher affinity for complementary single stranded DNA (ssDNA). These compounds are also able to form triple helices wherein a first PNA strand binds with RNA or ssDNA and a second PNA strand binds with the resulting double helix or with the first PNA strand. PNAs generally possess no significant charge and are water soluble, which facilitates cellular uptake. Moreover, PNAs contain amides of non-biological amino acids, making them biostable and resistant to enzymatic degradation, for example, by proteases.

Accordingly, PNAs can ideally be used to target RNA and ssDNA to produce antisense-type gene regulating moieties. Reagents that bind sequence-specifically to dsDNA, RNA, or ssDNA have applications as gene targeted drugs useful for modulating metabolic processes such as metabolic regulatory dysfunctions, such as cancer.

Alterations in the cellular genes which directly or indirectly control cell growth and differentiation are considered to be the main cause of cancer. There are some thirty families of genes, called oncogenes, which are implicated in human tumor formation. Members of one such family, the ras gene family, are frequently found to be mutated in human tumors. In their normal state, proteins produced by the ras genes are thought to be involved in normal cell growth and maturation. Mutation of the ras gene, causing an amino acid alteration at one of three critical positions in the protein product, results in conversion to a form which is implicated in tumor formation. A gene having such a mutation is said to be "activated." It is thought that such a point mutation leading to ras activation can be induced by carcinogens or other environmental factors. Over 90% of pancreatic adenocarcinomas, about 50% of adenomas and adenocarcinomas of the colon, about 50% of adenocarcinomas of the lung and carcinomas of the thyroid, and a large fraction

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of malignancies of the blood such as acute myeloid leukemia and myelodysplastic syndrome have been found to contain activated ras oncogenes. Overall, some 10 to 20% of human tumors have a mutation in one of the three ras genes (H-ras, 5 K-ras, or N-ras).

It is presently believed that inhibiting expression of activated oncogenes in a particular tumor cell might force the cell back into a more normal growth habit. For example, Feramisco et al., *Nature*, 314:639-642, 1985, 10 demonstrated that if cells transformed to a malignant state with an activated ras gene are microinjected with antibody which binds to the protein product of the ras gene, the cells slow their rate of proliferation and adopt a more normal appearance. This has been interpreted as support for the 15 involvement of the product of the activated ras gene in the uncontrolled growth typical of cancer cells.

Antisense oligonucleotide inhibition of oncogenes has proven to be a useful tool in understanding the roles of various oncogene families. "Antisense oligonucleotides" 20 refers to small oligonucleotides which are complementary to the "sense" or coding strand of a given gene, and as a result are also complementary to, and thus able to specifically hybridize with, the mRNA transcript of the gene. Holt et al., *Mol. Cell Biol.*, 8, 963-973, 1988, have shown that 25 antisense oligonucleotides hybridizing specifically with mRNA transcripts of the oncogene c-myc, when added to cultured HL60 leukemic cells, inhibit proliferation and induce differentiation. Anfossi et al., *Proc. Natl. Acad. Sci.*, 86, 3379-3383, 1989, have shown that antisense oligonucleotides 30 specifically hybridizing with mRNA transcripts of the c-myb oncogene inhibit proliferation of human myeloid leukemia cell lines. Wickstrom et al., *Proc. Nat. Acad. Sci.*, 85, 1028-1032, 1988, have shown that expression of the protein product of the c-myc oncogene as well as proliferation of HL60 35 cultured leukemic cells are inhibited by antisense oligonucleotides hybridizing specifically with c-myc mRNA. U.S. Patent 4,871,838 (Bos et al.) discloses oligonucleotides

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complementary to a mutation in codon 13 of N-ras to detect said mutation.

In all these cases, instability of unmodified oligonucleotides has been a major problem, as they are subject to degradation by cellular enzymes. PCT/US88/01024 (Zon et al.) discloses phosphorothioate oligonucleotide analogs hybridizable to the translation initiation region of the amplified c-myc oncogene to inhibit HL-60 leukemia cell growth and DNA synthesis in these cells. Tidd et al., *Anti-Cancer Drug Design*, 3, 117-127, 1988, evaluated antisense oligonucleotide methylphosphonate analogs hybridizing specifically to the activated N-ras oncogene and found that while they were resistant to biochemical degradation and were nontoxic in cultured human HT29 cells, they did not inhibit N-ras gene expression and had no effect on these cells. Chang et al., *Anti-Cancer Drug Design*, 4, 221-232, 1989, showed that both methylphosphonate and phosphorothioate analogs of oligonucleotides hybridizing specifically to mRNA transcripts of the Balb-ras gene could inhibit translation of the protein product of this gene *in vitro*. Because the antisense oligonucleotides and oligonucleotide analogs used by Chang et al. hybridize specifically with the translation initiation region of the ras gene, the binding ability of these oligonucleotides to normal (wild-type) vs. mutated (activated) ras genes was not compared.

The H-ras gene has recently been implicated in a serious cardiac arrhythmia called long Q-T syndrome, a hereditary condition which often causes sudden death if treatment is not given immediately. Frequently there are no symptoms prior to the onset of the erratic heartbeat. Whether the H-ras gene is precisely responsible for long Q-T syndrome is unclear. However, there is an extremely high correlation between inheritance of this syndrome and the presence of a particular variant of the chromosome 11 region surrounding the H-ras gene. This makes the H-ras gene an excellent indicator of increased risk of sudden cardiac death due to the long Q-T syndrome.

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There is a great desire to provide compositions of matter which can modulate the expression of the ras gene, and particularly to provide compositions of matter which specifically modulate the expression of the activated form of 5 the ras gene. It is greatly desired to provide methods of diagnosis and detection of the ras gene in animals. It is also desired to provide methods of diagnosis and treatment of conditions arising from ras gene activation. In addition, improved research kits and reagents for detection and study 10 of the ras gene are desired.

SUMMARY OF THE INVENTION

The present invention provides oligomers comprising peptide nucleic acids (PNAs), that bind complementary ssDNA and RNA strands through their oligoribonucleotide ligands 15 which are linked to a peptide backbone. The sequence of the oligoribonucleotide ligands specifies the target to which they bind.

In accordance with the present invention, oligomers are provided that are specifically hybridizable with DNA or 20 RNA deriving from the human ras gene. Such oligomers are conveniently and desirably presented in a pharmaceutically acceptable carrier.

Other aspects of the invention are directed to methods for modulating the expression of the human ras gene 25 in cells or tissues and for specifically modulating the expression of the activated ras gene in cells or tissues suspected of harboring a mutation leading to such activation. Additional aspects of the invention are directed to methods of detection of the ras gene in cells or tissues and specific 30 detection of the activated ras gene in cells or tissues suspected of harboring said mutated gene. Such methods comprise contacting cells or tissues suspected of containing the human ras gene with oligomers in accordance with the invention in order to interfere with the effect of or detect 35 said gene.

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Other aspects of the invention are directed to methods for diagnostics and therapeutics of animals suspected of having a mutation leading to activation of the ras gene. Such methods comprise contacting the animal or cells or 5 tissues or a bodily fluid from the animal with oligomers in accordance with the invention in order to modulate the expression of this gene, to treat conditions arising from activation of this gene, or to effect a diagnosis thereof.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

10 Malignant tumors develop through a series of stepwise, progressive changes that lead to the loss of growth control characteristic of cancer cells, i.e., continuous unregulated proliferation, the ability to invade surrounding tissues, and the ability to metastasize to different organ 15 sites. Carefully controlled *in vitro* studies have helped define the factors that characterize the growth of normal and neoplastic cells and have led to the identification of specific proteins that control cell growth and differentiation. In addition, the ability to study cell 20 transformation in carefully controlled, quantitative *in vitro* assays has led to the identification of specific genes capable of inducing the transformed cell phenotype. Such cancer-causing genes, or oncogenes, are believed to acquire transformation-inducing properties through mutations leading 25 to changes in the regulation of expression of their protein products. In some cases such changes occur in non-coding DNA regulatory domains, such as promoters and enhancers, leading to alterations in the transcriptional activity of oncogenes, resulting in over- or under-expression of their gene 30 products. In other cases, gene mutations occur within the coding regions of oncogenes, leading to the production of altered gene products that are inactive, overactive, or exhibit an activity that is different from the normal (wild-type) gene product.

35 To date, more than 30 cellular oncogene families have been identified. These genes can be categorized on the

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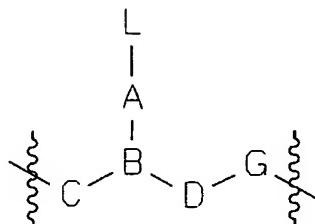
basis of both their subcellular location and the putative mechanism of action of their protein products. The ras oncogenes are members of a gene family which encode related proteins that are localized to the inner face of the plasma membrane. ras proteins have been shown to be highly conserved at the amino acid level, to bind GTP with high affinity and specificity, and to possess GTPase activity. Although the cellular function of ras gene products is unknown, their biochemical properties, along with their significant sequence homology with a class of signal-transducing proteins known as GTP binding proteins, or G proteins, suggest that ras gene products play a fundamental role in basic cellular regulatory functions relating to the transduction of extracellular signals across plasma membranes.

Three ras genes, designated H-ras, K-ras, and N-ras, have been identified in the mammalian genome. Mammalian ras genes acquire transformation-inducing properties by single point mutations within their coding sequences. Mutations in naturally occurring ras oncogenes have been localized to codons 12, 13, and 61. The most commonly detected activating ras mutation found in human tumors is in codon 12 of the H-ras gene in which a base change from GGC to GTC results in a glycine-to-valine substitution in the GTPase regulatory domain of the ras protein product. This single amino acid change is thought to abolish normal control of ras protein function, thereby converting a normally regulated cell protein to one that is continuously active. It is believed that such deregulation of normal ras protein function is responsible for the transformation from normal to malignant growth.

The present invention provides oligomers for inhibition of human ras gene expression.

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Oligomers of the present invention are comprised of at least one subunit having the formula:

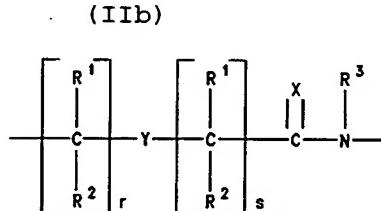
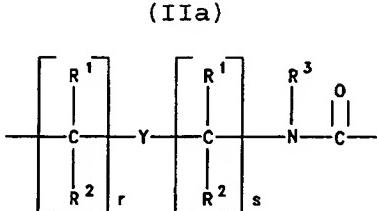
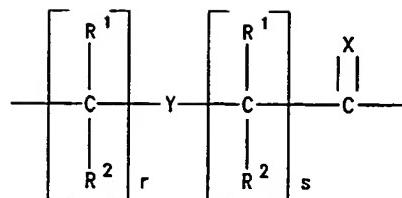
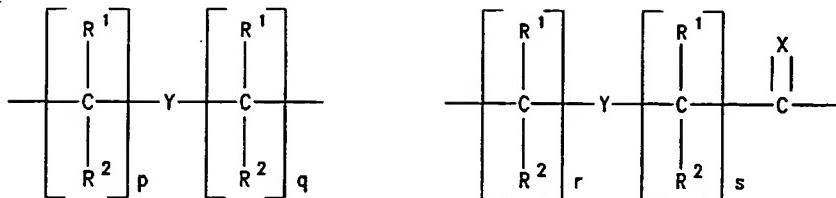


(I)

wherein:

- 5 L is one of the adenine, thymine, cytosine or guanine heterocyclic bases of the oligomer;
- C is $(CR^6R^7)_y$, where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are independently selected from the group consisting of hydrogen, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, NR^3R^4 and SR^5 , where each of R^3 and R^4 is independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio and amino; and R^5 is hydrogen, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6) alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;
- 10 D is $(CR^6R^7)_z$, where R^6 and R^7 are as defined above;
- 20 each of y and z is zero or an integer from 1 to 10, the sum $y + z$ being greater than 2 but not more than 10;
- G is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;
- each pair of A and B is selected such that:
 - 25 (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or
 - (b) A is a group of formula (IId) and B is CH;

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where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5, the sum p+q being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum r+s being not more than 10; and

each R¹ and R² is independently selected from the group consisting of hydrogen, (C₁-C₄)alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen.

The term peptide nucleic acid subunits (PNA subunit), as used herein, refers to units in accordance with Formula I, which can form oligomers. Preferred oligomers of the present invention are oligomers in which substantially all subunits of the oligomer are subunits as described in Formula I, i.e. PNA subunits. Oligomers of the present invention may also comprise one or more subunits which are naturally occurring nucleotides or nucleotide analogs as long as at least one subunit satisfies Formula I. Thus, oligomers as used herein may refer to a range of oligomers from oligomers comprising only one PNA subunit as defined in

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Formula I to oligomers in which every subunit is a PNA subunit as defined in Formula I.

Those subunits which are not PNA subunits preferably comprise naturally occurring bases, sugars, and 5 intersugar (backbone) linkages as well as non-naturally occurring portions which function similarly to naturally occurring portions. Sequences of oligomers of the present invention are defined by reference to the L group (for PNA subunits) or nucleobase (for nucleotide subunits) at 10 a given position. Thus, for a given oligomer, the nomenclature is modeled after traditional nucleotide nomenclature, identifying each PNA subunit by the identity of its L group such as the heterocycles adenine (A), thymine (T), guanine (G) and cytosine (C) and identifying nucleotides 15 or nucleosides by these same heterocycle residing on the sugar backbone. The sequences are conveniently provided in traditional 5' to 3' or amino to carboxy orientation.

Oligomers of the present invention may range in size from about 5 to about 50 subunits in length. In other 20 embodiments of the present invention, oligomers may range in size from about 10 to about 30 subunits in length. In still other embodiments of the present invention oligomers may range in size from about 10 to about 25 subunits in length. In yet further embodiments of the present invention, 25 oligomers may range in size from about 12 to about 20 subunits in length.

The preparation of protein nucleic acid oligomers is known in the art, such as is described in PCT/EP 92/01219 filed May 22, 1992, which is incorporated by reference herein 30 in its entirety.

Briefly, the principle of anchoring molecules onto a solid matrix, which helps in accounting for intermediate products during chemical transformations, is known as Solid-Phase Synthesis or Merrifield Synthesis (see, e.g., 35 Merrifield, *J. Am. Chem. Soc.*, 1963, 85, 2149 and *Science*, 1986, 232, 341). Established methods for the stepwise or fragmentwise solid-phase assembly of amino acids into

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peptides normally employ a beaded matrix of slightly cross-linked styrene-divinylbenzene copolymer, the cross-linked copolymer having been formed by the pearl polymerization of styrene monomer to which has been added a mixture of 5 divinylbenzenes. A level of 1-2% cross-linking is usually employed. Such a matrix also can be used in solid-phase PNA synthesis in accordance with the present invention.

Concerning the initial functionalization of the solid phase, more than fifty methods have been described in 10 connection with traditional solid-phase peptide synthesis (see, e.g., Barany and Merrifield in "The Peptides" Vol. 2, Academic Press, New York, 1979, pp. 1-284, and Stewart and Young, "Solid Phase Peptide Synthesis", 2nd Ed., Pierce Chemical Company, Illinois, 1984). Reactions for the 15 introduction of chloromethyl functionality (Merrifield resin; via a chloromethyl methyl ether/SnCl₄ reaction), aminomethyl functionality (via an N-hydroxymethylphthalimide reaction; see, Mitchell, et al., *Tetrahedron Lett.*, 1976, 3795), and benzhydryl amino functionality (Pietta, et al., *J. Chem. Soc.*, 20 1970, 650) are the most widely applied. Regardless of its nature, the purpose of the functionality is normally to form an anchoring linkage between the copolymer solid support and the C-terminus of the first amino acid to be coupled to the solid support. As will be recognized, anchoring linkages 25 also can be formed between the solid support and the amino acid N-terminus. It is generally convenient to express the "concentration" of a functional group in terms of millimoles per gram (mmol/g). Other reactive functionalities which have been initially introduced include 4-methylbenzhydryl amino and 30 4-methoxybenzhydryl amino. All of these established methods are in principle useful within the context of the present invention. Preferred methods for PNA synthesis employ aminomethyl as the initial functionality, in that aminomethyl is particularly advantageous with respect to the 35 incorporation of "spacer" or "handle" groups, owing to the reactivity of the amino group of the aminomethyl functionality with respect to the essentially quantitative

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formation of amide bonds to a carboxylic acid group at one end of the spacer-forming reagent. A vast number of relevant spacer- or handle-forming bifunctional reagents have been described (see, Barany, et al., *Int. J. Peptide Protein Res.*, 5 1987, 30, 705), especially reagents which are reactive towards amino groups such as found in the aminomethyl function. Representative bifunctional reagents include 4-(haloalkyl)aryl-lower alkanoic acids such as 4-(bromomethyl)phenylacetic acid, Boc-aminoacyl-4-(oxymethyl)aryl-lower alkanoic acids such as Boc-aminoacyl-4-(oxymethyl)phenylacetic acid, N-Boc-p-acylbenzhydrylamines such as N-Boc-p-glutaroylbenzhydrylamine, N-Boc-4'-lower alkyl-p-acylbenzhydrylamines such as N-Boc-4'-methyl-p-glutaroylbenzhydrylamine, N-Boc-4'-lower alkoxy-p-acylbenzhydrylamines such as N-Boc-4'-methoxy-p-glutaroyl-benzhydrylamine, and 4-hydroxymethylphenoxyacetic acid. One type of spacer group particularly relevant within the context of the present invention is the phenylacetamidomethyl (Pam) handle (Mitchell and Merrifield, *J. Org. Chem.*, 1976, 41, 20 2015) which, deriving from the electron withdrawing effect of the 4-phenylacetamidomethyl group, is about 100 times more stable than the classical benzyl ester linkage towards the Boc-amino deprotection reagent trifluoroacetic acid (TFA).

Certain functionalities (e.g., benzhydrylamo, 4-methylbenzhydrylamo and 4-methoxybenzhydrylamo) which may be incorporated for the purpose of cleavage of a synthesized PNA chain from the solid support such that the C-terminal of the PNA chain is in amide form, require no introduction of a spacer group. Any such functionality may advantageously be 30 employed in the context of the present invention.

An alternative strategy concerning the introduction of spacer or handle groups is the so-called "preformed handle" strategy (see, Tam, et al., *Synthesis*, 1979, 955-957), which offers complete control over coupling of the first amino acid, and excludes the possibility of complications arising from the presence of undesired functional groups not related to the peptide or PNA

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synthesis. In this strategy, spacer or handle groups, of the same type as described above, are reacted with the first amino acid desired to be bound to the solid support, the amino acid being N-protected and optionally protected at the 5 other side-chains which are not relevant with respect to the growth of the desired PNA chain. Thus, in those cases in which a spacer or handle group is desirable, the first amino acid to be coupled to the solid support can either be coupled to the free reactive end of a spacer group which has been 10 bound to the initially introduced functionality (for example, an aminomethyl group) or can be reacted with the spacer-forming reagent. The space-forming reagent is then reacted with the initially introduced functionality. Other useful anchoring schemes include the "multidetachable" resins (Tam, 15 et al., *Tetrahedron Lett.*, 1979, 4935 and *J. Am. Chem. Soc.*, 1980, 102, 611; Tam, *J. Org. Chem.*, 1985, 50, 5291), which provide more than one mode of release and thereby allow more flexibility in synthetic design.

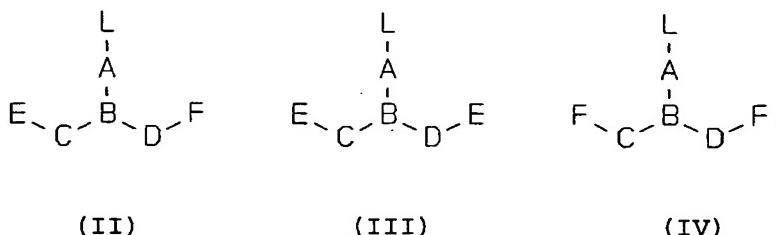
Suitable choices for N-protection are the tert-butyloxycarbonyl (Boc) group (Carpino, *J. Am. Chem. Soc.*, 1957, 79, 4427; McKay, et al., *J. Am. Chem. Soc.*, 1957, 79, 4686; Anderson, et al., *J. Am. Chem. Soc.*, 1957, 79, 6180) normally in combination with benzyl-based groups for the protection of side chains, and the 9-fluorenylmethoxy-25 carbonyl (Fmoc) group (Carpino, et al., *J. Am. Chem. Soc.*, 1970, 92, 5748 and *J. Org. Chem.*, 1972, 37, 3404), normally in combination with tert-butyl (tBu) for the protection of any side chains, although a number of other possibilities exist which are well known in conventional solid-phase 30 peptide synthesis. Thus, a wide range of other useful amino protecting groups exist, some of which are Adoc (Hass, et al., *J. Am. Chem. Soc.*, 1966, 88, 1988), Bpoc (Sieber, *Helv. Chem. Acta.*, 1968, 51, 614), Mcb (Brady, et al., *J. Org. Chem.*, 1977, 42, 143), Bic (Kemp, et al., *Tetrahedron*, 1975, 35 4624), the o-nitrophenylsulfenyl (Nps) (Zervas, et al., *J. Am. Chem. Soc.*, 1963, 85, 3660), and the dithiasuccinoyl (Dts) (Barany, et al., *J. Am. Chem. Soc.*, 1977, 99, 7363).

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These amino protecting groups, particularly those based on the widely-used urethane functionality, successfully prohibit racemization (mediated by tautomerization of the readily formed oxazolinone (azlactone) intermediates (Goodman, et al., *J. Am. Chem. Soc.*, 1964, 86, 2918)) during the coupling of most α -amino acids. In addition to such amino protecting groups, a whole range of otherwise "worthless" nonurethane-type of amino protecting groups are applicable when assembling PNA molecules, especially those built from achiral units. Thus, not only the above-mentioned amino protecting groups (or those derived from any of these groups) are useful within the context of the present invention, but virtually any amino protecting group which largely fulfills the following requirements: (1) stability to mild acids (not significantly attacked by carboxyl groups); (2) stability to mild bases or nucleophiles (not significantly attacked by the amino group in question); (3) resistance to acylation (not significantly attacked by activated amino acids). Additionally: (4) the protecting group must be close to quantitatively removable, without serious side reactions, and (5) the optical integrity, if any, of the incoming amino acid should preferably be highly preserved upon coupling. Finally, the choice of side-chain protecting groups, in general, depends on the choice of the amino protecting group, since the protection of side-chain functionalities must withstand the conditions of the repeated amino deprotection cycles. This is true whether the overall strategy for chemically assembling PNA molecules relies on, for example, differential acid stability of amino and side-chain protecting groups (such as is the case for the above-mentioned "Boc-benzyl" approach) or employs an orthogonal, that is, chemoselective, protection scheme (such as is the case for the above-mentioned "Fmoc-tBu" approach), Following coupling of the first amino acid, the next stage of solid-phase synthesis is the systematic elaboration of the desired PNA chain to incorporate additional subunits using monomer synthons. Novel monomer

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synthons may be selected from the group consisting of amino acids, diacids and diamines having general formulae:



wherein L, A, B, C and D are as defined above, except that
 5 any amino groups therein may be protected by amino protecting groups; E is COOH, CSOH, SOOH, SO₂OH or an activated derivative thereof; and F is NHR³ or NPgR³, where R³ is as defined above and Pg is an amino protecting group. This elaboration involves repeated deprotection/coupling cycles.
 10 The temporary protecting group, such as a Boc or Fmoc group, on the last-coupled amino acid is quantitatively removed by a suitable treatment, for example, by acidolysis, such as with trifluoroacetic acid, in the case of Boc, or by base treatment, such as with piperidine, in the case of Fmoc, so
 15 as to liberate the N-terminal amine function.

The next desired N-protected amino acid is then coupled to the N-terminal of the last-coupled amino acid. This coupling of the C-terminal of an amino acid with the N-terminal of the last-coupled amino acid can be achieved in
 20 several ways. For example, it can be bound by providing the incoming amino acid in a form with the carboxyl group activated by any of several methods, including the initial formation of an active ester derivative such as a 2,4,5-trichlorophenyl ester (Pless, et al., *Helv. Chim. Acta*, 1963, 46, 1609), a phthalimido ester (Nefkens, et al., *J. Am. Chem. Soc.*, 1961, 83, 1263), a pentachlorophenyl ester (Kupryszewski, *Roczn. Chem.*, 1961, 35, 595), a pentafluorophenyl ester (Kovacs, et al., *J. Am. Chem. Soc.*, 1963, 85, 183), an o-nitrophenyl ester (Bodanzsky, *Nature*, 1955, 175, 25 685), an imidazole ester (Li, et al., *J. Am. Chem. Soc.*, 1970, 92, 7608), and a 3-hydroxy-4-oxo-3,4-dihydroquinazoline (Dhb_t-OH) ester (Konig, et al., *Chem. Ber.*, 1973, 103, 2024

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and 2034), or the initial formation of an anhydride such as a symmetrical anhydride (Wieland, et al., *Angew. Chem., Int. Ed. Engl.*, 1971, 10, 336). Alternatively, the carboxyl group of the incoming amino acid can be reacted directly with the 5 N-terminal of the last-coupled amino acid with the assistance of a condensation reagent such as, for example, dicyclohexylcarbodiimide (Sheehan, et al., *J. Am. Chem. Soc.*, 1955, 77, 1067) or derivatives thereof. Benzotriazolyl N-oxytrisdimethylaminophosphonium hexafluorophosphate (BOP), 10 "Castro's reagent" (see, e.g., Rivaille, et al., *Tetrahedron*, 1980, 36, 3413) is recommended when assembling PNA molecules containing secondary amino groups. Finally, activated PNA monomers analogous to the recently-reported amino acid fluorides (Carpino, *J. Am. Chem. Soc.*, 1990, 112, 9651) hold 15 considerable promise to be used in PNA synthesis as well.

Following assembly of the desired PNA chain, including protecting groups, the next step will normally be deprotection of the amino acid moieties of the PNA chain and cleavage of the synthesized PNA from the solid support. 20 These processes can take place substantially simultaneously, thereby providing the free PNA molecule in the desired form. Alternatively, in cases in which condensation of two separately synthesized PNA chains is to be carried out, it is possible by choosing a suitable spacer group at the start of 25 the synthesis to cleave the desired PNA chains from their respective solid supports (both peptide chains still incorporating their side-chain protecting groups) and finally removing the side-chain protecting groups after, for example, coupling the two side-chain protected peptide chains to form 30 a longer PNA chain.

In the above-mentioned "Boc-benzyl" protection scheme, the final deprotection of side-chains and release of the PNA molecule from the solid support is most often carried out by the use of strong acids such as anhydrous HF 35 (Sakakibara, et al., *Bull. Chem. Soc. Jpn.*, 1965, 38, 4921), boron tris (trifluoroacetate) (Pless, et al., *Helv. Chim. Acta*, 1973, 46, 1609), and sulfonic acids such as

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trifluoromethanesulfonic acid and methanesulfonic acid (Yajima, et al., *J. Chem. Soc., Chem. Comm.*, 1974, 107). This conventional strong acid (e.g., anhydrous HF) deprotection method, produces very reactive carbocations that 5 may lead to alkylation and acylation of sensitive residues in the PNA chain. Such side-reactions are only partly avoided by the presence of scavengers such as anisole, phenol, dimethyl sulfide, and mercaptoethanol and, therefore, the sulfide-assisted acidolytic S_N2 deprotection method (Tam, et 10 al., *J. Am. Chem. Soc.*, 1983, 105, 6442 and *J. Am. Chem. Soc.*, 1986, 108, 5242), the so-called "low", which removes the precursors of harmful carbocations to form inert sulfonium salts, is frequently employed in peptide and PNA synthesis, either solely or in combination with "high" 15 methods. Less frequently, in special cases, other methods used for deprotection and/or final cleavage of the PNA-solid support bond are, for example, such methods as base-catalyzed alcoholysis (Barton, et al., *J. Am. Chem. Soc.*, 1973, 95, 4501), and ammonolysis as well as hydrazinolysis (Bodanszky, 20 et al., *Chem. Ind.*, 1964 1423), hydrogenolysis (Jones, *Tetrahedron Lett.* 1977 2853 and Schlatter, et al., *Tetrahedron Lett.* 1977 2861)), and photolysis (Rich and Gurwara, *J. Am. Chem. Soc.*, 1975 97, 1575)).

Finally, in contrast with the chemical synthesis of 25 "normal" peptides, stepwise chain building of achiral PNAs such as those based on aminoethylglycyl backbone units can start either from the N-terminus or the C-terminus, because the coupling reactions are free of racemization. Those skilled in the art will recognize that whereas syntheses 30 commencing at the C-terminus typically employ protected amine groups and free or activated acid groups, syntheses commencing at the N-terminus typically employ protected acid groups and free or activated amine groups.

Based on the recognition that most operations are 35 identical in the synthetic cycles of solid-phase peptide synthesis (as is also the case for solid-phase PNA synthesis), a new matrix, PEPS, was recently introduced

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(Berg, et al., *J. Am. Chem. Soc.*, 1989, 111, 8024 and International Patent Application WO 90/02749) to facilitate the preparation of large numbers of peptides. This matrix is comprised of a polyethylene (PE) film with pendant long-chain polystyrene (PS) grafts (molecular weight on the order of 10⁶). The loading capacity of the film is as high as that of a beaded matrix, but PEPS has the additional flexibility to suit multiple syntheses simultaneously. Thus, in a new configuration for solid-phase peptide synthesis, the PEPS film is fashioned in the form of discrete, labeled sheets, each serving as an individual compartment. During all the identical steps of the synthetic cycles, the sheets are kept together in a single reaction vessel to permit concurrent preparation of a multitude of peptides at a rate close to that of a single peptide by conventional methods. It was reasoned that the PEPS film support, comprising linker or spacer groups adapted to the particular chemistry in question, should be particularly valuable in the synthesis of multiple PNA molecules, these being conceptually simple to synthesize since only four different reaction compartments are normally required, one for each of the four "pseudo-nucleotide" units. Thus, the PEPS film support has been successfully tested in a number of PNA syntheses carried out in a parallel and substantially simultaneous fashion. The yield and quality of the products obtained from PEPS were comparable to those obtained by using the traditional polystyrene beaded support. Also, experiments with other geometries of the PEPS polymer such as, for example, non-woven felt, knitted net, sticks or microwellplates have not indicated any limitations of the synthetic efficacy.

Two other methods proposed for the simultaneous synthesis of large numbers of peptides also apply to the preparation of multiple, different PNA molecules. The first of these methods (Geysen, et al., *Proc. Natl. Acad. Sci. USA*, 1984, 81, 3998) utilizes acrylic acid-grafted polyethylene-rods and 96-microtiter wells to immobilize the growing peptide chains and to perform the compartmentalized

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synthesis. While highly effective, the method is only applicable on a microgram scale. The second method (Houghten, *Proc. Natl. Acad. Sci. USA*, 1985, 82, 5131) utilizes a "tea bag" containing traditionally-used polymer beads. Other relevant proposals for multiple peptide or PNA synthesis in the context of the present invention include the simultaneous use of two different supports with different densities (Tregear, in "*Chemistry and Biology of Peptides*", J. Meienhofer, ed., Ann Arbor Sci. Publ., Ann Arbor, 1972 pp. 175-178), combining of reaction vessels via a manifold (Gorman, *Anal. Biochem.*, 1984, 136, 397), multicolumn solid-phase synthesis (e.g. Krchnak, et al., *Int. J. Peptide Protein Res.*, 1989, 33, 209), and Holm and Meldal, in "*Proceedings of the 20th European Peptide Symposium*", G. Jung and E. Bayer, eds., Walter de Gruyter & Co., Berlin, 1989 pp. 208-210), and the use of cellulose paper (Eichler, et al., *Collect. Czech. Chem. Commun.*, 1989, 54, 1746).

While the conventional cross-linked styrene/divinylbenzene copolymer matrix and the PEPS support are presently preferred in the context of solid-phase PNA synthesis, a non-limiting list of examples of solid supports which may be of relevance are: (1) Particles based upon copolymers of dimethylacrylamide cross-linked with N,N'-bisacryloylenediamine, including a known amount of N-tertbutoxycarbonyl-beta-alanyl-N'-acryloylhexamethylenediamine. Several spacer molecules are typically added via the beta alanyl group, followed thereafter by the amino acid residue subunits. Also, the beta alanyl-containing monomer can be replaced with an acryloyl sarcosine monomer during polymerization to form resin beads. The polymerization is followed by reaction of the beads with ethylenediamine to form resin particles that contain primary amines as the covalently linked functionality. The polyacrylamide-based supports are relatively more hydrophilic than are the polystyrene-based supports and are usually used with polar aprotic solvents including dimethylformamide, dimethylacetamide, N-methylpyrrolidone and the

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like (see Atherton, et al., *J. Am. Chem. Soc.*, 1975, 97, 6584, *Bioorg. Chem.* 1979, 8, 351), and J.C.S. Perkin I 538 (1981)); (2) a second group of solid supports is based on silica-containing particles such as porous glass beads and 5 silica gel. One example is the reaction product of trichloro-[3-(4-chloromethyl)phenyl]propylsilane and porous glass beads (see Parr and Grohmann, *Angew. Chem. Internal. Ed.* 1972, 11, 314) sold under the trademark "PORASIL E" by Waters Associates, Framingham, MA, USA. Similarly, a mono ester of 10 1,4-dihydroxymethylbenzene and silica (sold under the trademark "BIOPAK" by Waters Associates) has been reported to be useful (see Bayer and Jung, *Tetrahedron Lett.*, 1970, 4503); (3) a third general type of useful solid supports can be termed composites in that they contain two major 15 ingredients: a resin and another material that is also substantially inert to the organic synthesis reaction conditions employed. One exemplary composite (see Scott, et al., *J. Chrom. Sci.*, 1971, 9, 577) utilized glass particles coated with a hydrophobic, cross-linked styrene polymer 20 containing reactive chloromethyl groups, and was supplied by Northgate Laboratories, Inc., of Hamden, CT, USA. Another exemplary composite contains a core of fluorinated ethylene polymer onto which has been grafted polystyrene (see Kent and Merrifield, *Israel J. Chem.* 1978, 17, 243) and van 25 Rietschoten in "Peptides 1974", Y. Wolman, Ed., Wiley and Sons, New York, 1975, pp. 113-116); and (4) contiguous solid supports other than PEPS, such as cotton sheets (Lebl and Eichler, *Peptide Res.* 1989, 2, 232) and hydroxypropylacrylate-coated polypropylene membranes (Daniels, et al., *Tetrahedron Lett.* 1989, 4345), are suited for PNA synthesis 30 as well.

Whether manually or automatically operated, solid-phase PNA synthesis in the context of the present invention is normally performed batchwise. However, most of the syntheses may equally well be carried out in the continuous-flow 35 mode, where the support is packed into columns (Bayer, et al., *Tetrahedron Lett.*, 1970, 4503 and Scott, et al., *J.*

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Chromatogr. Sci., 1971, 9, 577). With respect to continuous-flow solid-phase synthesis, the rigid poly(dimethylacrylamide)-Kieselguhr support (Atherton, et al., *J. Chem. Soc. Chem. Commun.*, 1981, 1151) appears to be particularly successful, 5 but another valuable configuration concerns the one worked out for the standard copoly(styrene-1%-divinylbenzene) support (Krchnak, et al., *Tetrahedron Lett.*, 1987, 4469).

While the solid-phase technique is presently preferred in the context of PNA synthesis, other 10 methodologies or combinations thereof, for example, in combination with the solid-phase technique, apply as well: (1) the classical solution-phase methods for peptide synthesis (e.g., Bodanszky, "Principles of Peptide Synthesis", Springer-Verlag, Berlin-New York 1984), either by 15 stepwise assembly or by segment/fragment condensation, are of particular relevance when considering especially large scale productions (gram, kilogram, and even tons) of PNA compounds; (2) the so-called "liquid-phase" strategy, which utilizes soluble polymeric supports such as linear polystyrene 20 (Shemyakin, et al., *Tetrahedron Lett.*, 1965, 2323) and polyethylene glycol (PEG) (Mutter and Bayer, *Angew. Chem., Int. Ed. Engl.*, 1974, 13, 88), is useful; (3) random polymerization (see, e.g., Odian, "Principles of Polymerization", McGraw-Hill, New York (1970)) yielding 25 mixtures of many molecular weights ("polydisperse") peptide or PNA molecules are particularly relevant for purposes such as screening for antiviral effects; (4) a technique based on the use of polymer-supported amino acid active esters (Fridkin, et al., *J. Am. Chem. Soc.*, 1965, 87, 4646), 30 sometimes referred to as "inverse Merrifield synthesis" or "polymeric reagent synthesis", offers the advantage of isolation and purification of intermediate products, and may thus provide a particularly suitable method for the synthesis of medium-sized, optionally protected, PNA molecules, that 35 can subsequently be used for fragment condensation into larger PNA molecules; (5) it is envisaged that PNA molecules may be assembled enzymatically by enzymes such as proteases

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or derivatives thereof with novel specificities (obtained, for example, by artificial means such as protein engineering). Also, one can envision the development of "PNA ligases" for the condensation of a number of PNA fragments 5 into very large PNA molecules; (6) since antibodies can be generated to virtually any molecule of interest, the recently developed catalytic antibodies (abzymes), discovered simultaneously by the groups of Lerner (Tramantano, et al., *Science*, 1986, 234, 1566) and of Schultz (Pollack, et al., 10 *Science*, 1986, 234, 1570), should also be considered as potential candidates for assembling PNA molecules. Thus, there has been considerable success in producing abzymes catalyzing acyl-transfer reactions (see for example Shokat, et al., *Nature*, 1989, 338, 269) and references therein).

15 Finally, completely artificial enzymes, very recently pioneered by Stewart's group (Hahn, et al., *Science*, 1990, 248, 1544), may be developed to suit PNA synthesis. The design of generally applicable enzymes, ligases, and catalytic antibodies, capable of mediating specific coupling 20 reactions, should be more readily achieved for PNA synthesis than for "normal" peptide synthesis since PNA molecules will often be comprised of only four different amino acids (one for each of the four native nucleobases) as compared to the twenty natural by occurring (proteinogenic) amino acids 25 constituting peptides. In conclusion, no single strategy may be wholly suitable for the synthesis of a specific PNA molecule, and therefore, sometimes a combination of methods may work best.

Peptide nucleic acid oligomers hybridizable with, 30 or targeted to, *ras* genes such as *H-ras* and *K-ras* are provided by the present invention. By hybridizable is meant that at least 70% sequence homology is present. In preferred embodiments of the present invention, peptide nucleic acid oligomers have at least 85% sequence homology to a desired 35 target. In still more preferred embodiments of the present invention, peptide nucleic acid oligomers of the present

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invention are at least 95% homologous to a target of interest.

The oligomers of this invention are designed to be hybridizable with messenger RNA derived from the ras gene, 5 and especially from the H-ras and K-ras genes. Such hybridization, when accomplished, interferes with the normal roles of the messenger RNA to cause a loss of its function in the cell. The functions of messenger RNA to be interfered with include all vital functions such as translocation of the 10 RNA to the site for protein translation, actual translation of protein from the RNA, splicing of the RNA to yield one or more mRNA species, and possibly even independent catalytic activity which may be engaged in by the RNA. The overall effect of such interference with the RNA function is to 15 interfere with expression of the ras genes, and particularly the genes of H-ras and K-ras. The nucleic acid sequences of the three ras genes, while not identical, are known, and persons of ordinary skill in the art will be able to use this 20 invention as a guide in preparing oligomers hybridizable with all three ras genes.

The oligomers of this invention can be used in diagnostics, therapeutics and as research reagents and kits. Since the oligomers of this invention hybridize to the ras gene, sandwich and other assays can easily be constructed to 25 exploit this fact. Furthermore, since the oligomers of this invention hybridize preferentially to the mutant (activated) form of the ras oncogene, such assays can be devised for screening of cells and tissues for ras conversion from wild-type to activated form. Such assays can be utilized for 30 differential diagnosis of morphologically similar tumors, and for detection of increased risk of cancer stemming from ras gene activation. Provision of means for detecting hybridization of oligomers with the ras gene can routinely be accomplished. Such provision may include enzyme conjugation, 35 radiolabelling or any other suitable detection systems. Kits for detecting the presence or absence of ras or activated ras may also be prepared.

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A series of PNA oligomers targeted to the H-ras translation initiation codon (AUG), codon-12 point mutation or the stem and loop of the mRNA hairpin of activated H-ras were identified having specific sequences. The sequences, SEQ ID numbers and targets of these oligomers are shown in Table 1.

TABLE 1

	SEQUENCE	TARGET	SEQ ID NO:
	CCACACGGCCGGCGCC	codon 12	1
10	CTTATATTCCGTCATCGCTC	AUG	2
	TCCGTCATCGCTCCTCAGGG	AUG	3
	TGCCCACACCGACGGCGCCCACC	codon 12	4
	TTGCCACACCGACGGCGCCCACCA	codon 12	5
	CGACG	codon 12	6
15	CCGACGG	codon 12	7
	ACCGACGGC	codon 12	8
	GCCCCACACCGACGGCGCCCAC	codon 12	9
	CACCGACGGCG	codon 12	10
	ACACCGACGGCGC	codon 12	11
20	CACACCGACGGCGCC	codon 12	12
	CCACACCGACGGCGCC	codon 12	13
	CCCACACCGACGGCGCCCA	codon 12	14
	CACCAACCACC	hairpin stem	15
	GCGCCCACCA	hairpin stem	16
25	UUGCCCACAC	hairpin loop	17
	CACUCUUGCC	3' hairpin loop	18
	CACACCGACG	5' hairpin loop	19
	CGACGGCGCC	hairpin stem & loop	20
	CCACACCGACGGCGCC	codon 12	21
30	CACACCGACGGCGCC	codon 12	22
	CCCACACCGACGGCGCC	codon 12	23
	CCACACCGACGGCGCCCA	codon 12	24
	TATTCCGTCATCGCTCCTCA	AUG	25

A series of PNA oligomers complementary to the K-ras 5' untranslated region, 3'-untranslated region, translation initiation codon (AUG) and to coding regions,

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codon 12, 61 and 38 of the human K-ras gene, McGrath, J.P., et al., *Nature*, 304, 501-506 (1983) were identified having specific sequences. The sequences, SEQ ID numbers and targets of these oligomers are shown in Table 2.

5

TABLE 2

	SEQUENCE	TARGET	SEQ ID NO:
	CTGCCTCCGCCGCCGCGGCC	5' UTR/5' cap	26
	CAGTGCGCTGCGCCGCGCTCG	5' -UTR	27
	AGGCCTCTCTCCCGCACCTG	5' -UTR	28
10	TTCAGTCATTTCAGCAGGC	AUG	29
	TTATATTCAAGTCATTTCAG	AUG	30
	CAAGTTTATATTCAAGTCATT	AUG	31
	GCCTACGCCACCAGCTCCAAC	Codon 12 (WT)	32
	CTACGCCACCAGCTCCA	Codon 12 (WT)	33
15	GTACTCCTCTTGACCTGCTGT	Codon 61 (WT)	34
	CCTGTAGGAATCCTCTATTGT	Codon 38	35
	GGTAATGCTAAACAAATGC	3' -UTR	36
	GGAATACTGGCACTTCGAGG	3' -UTR	37
	TACGCCAACAGCTCC	Codon 12 (G→T mut.)	38
20	TTTCAGCAGGCCCTCTCTCC	5' -UTR/AUG	39

- Oligomers of the invention can be formulated in a pharmaceutical composition, which can include carriers, thickeners, diluents, buffers, preservatives, surface active agents and the like in addition to the oligonucleotide.
- 25 Pharmaceutical compositions also can include one or more active ingredients such as antimicrobial agents, anti-inflammatory agents, anesthetics, and the like in addition to oligomer.
- The pharmaceutical composition can be administered in a number of ways depending on whether local or systemic treatment is desired, and on the area to be treated. Administration can be topically (including ophthalmically, vaginally, rectally, intranasally), orally, by inhalation, or parenterally, for example by intravenous drip, subcutaneous, 35 intraperitoneal or intramuscular injection.

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Formulations for topical administration can include ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Coated condoms may also be useful.

- Compositions for oral administration include powders or granules, suspensions or solutions in water or non-aqueous media, capsules, sachets, or tablets.
- 10 Thickeners, flavorings, diluents, emulsifiers, dispersing aids or binders may be desirable.

Formulations for parenteral administration can include sterile aqueous solutions which also can contain buffers, diluents and other suitable additives.

15 Dosing is dependent on severity and responsiveness of the condition to be treated, but will normally be one or more doses per day, with course of treatment lasting from several days to several months or until a cure is effected or a diminution of disease state is achieved. Persons of ordinary skill can easily determine optimum dosages, dosing methodologies and repetition rates.

The following examples are provided for illustrative purposes only and are not intended to limit the invention.

25 **Example 1**

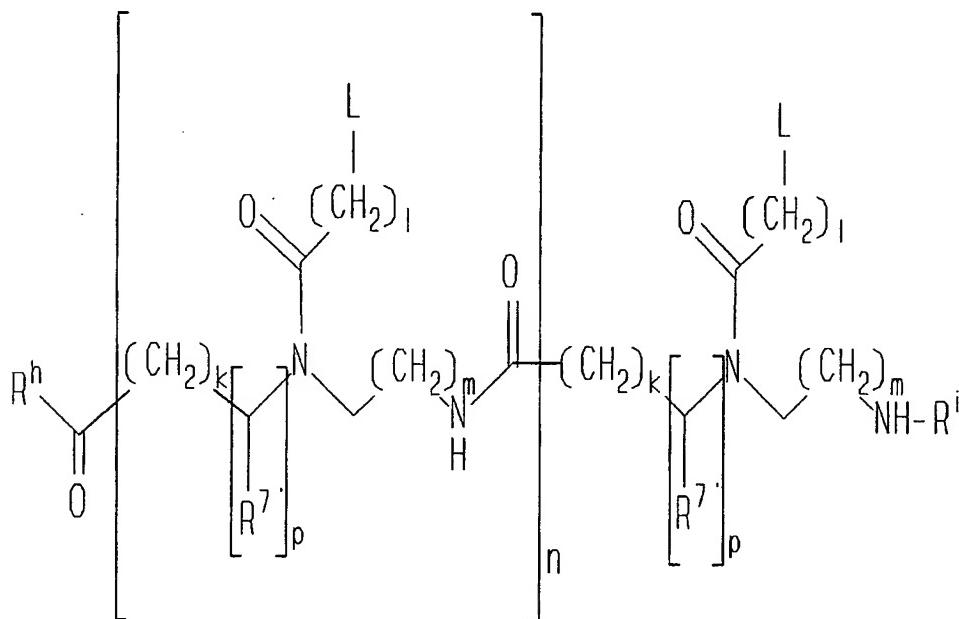
General Method for the Synthesis of PNA Oligomers

PNA subunits for oligomers of the invention were prepared generally in accordance with the methods disclosed by WO 92/20702, incorporated by reference herein and described above. For example, Benzyhydrylamine resin (initially loaded 0.28 mmol/gm with Boc-L-Lys(2-chlorobenzyloxycarbonyl)) was swollen in DMF and an excess of a monomer to be coupled was added, followed by dicyclohexylcarbodiimide (0.15M in 50% DMF in dichloromethane). The Boc deprotection was accomplished by trifluoroacetic acid treatment. The progress of the coupling reactions was

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monitored by quantitative ninhydrin analysis. The PNA was released from the resin using anhydrous HF under standard conditions. The products were purified using HPLC with acetonitrile-water (0.1%TFA) gradient and structure confirmed 5 by fast atom bombardment mass spectrometry.

PNA homopolymer has the structure:



wherein k is 1; m is 1; l is 1; p is 0; R^h is OH; Rⁱ is H; and n is the number of bases in the oligonucleotide sequence minus 1.

10 Example 2

PNA-DNA base pair recognition

The thermal stability of complexes between PNA oligomers of the invention and Watson-Crick complementary oligonucleotides when compared to DNA-RNA oligonucleotide 15 interactions illustrates that PNA-RNA base pair recognition

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DNA product of 145 base pairs corresponding to sequences -53 to +65 (relative to the translational initiation site) of normal and mutant H-ras, flanked by NheI and HindIII restriction endonuclease sites. The PCR product is gel 5 purified, precipitated, washed and resuspended in water using standard procedures.

PCR primers for the cloning of the *P. pyralis* (firefly) luciferase gene are designed such that the PCR product will code for the full-length luciferase protein with 10 the exception of the amino-terminal methionine residue, which would be replaced with two amino acids, an amino-terminal lysine residue followed by a leucine residue. The oligonucleotide PCR primers used for the cloning of the luciferase gene are used in standard PCR reactions using a 15 commercially available plasmid (pT3/T7-Luc) (Clontech), containing the luciferase reporter gene, as a template. These primers yield a product of approximately 1.9 kb corresponding to the luciferase gene, flanked by unique HindIII and BssHII restriction endonuclease sites. This 20 fragment is gel purified, precipitated, washed and resuspended in water using standard procedures.

To complete the assembly of the ras-luciferase fusion reporter gene, the ras and luciferase PCR products are digested with the appropriate restriction endonucleases and 25 cloned by three-part ligation into an expression vector containing the steroid-inducible mouse mammary tumor virus promotor MMTV using the restriction endonucleases NheI, HindIII and BssHII. The resulting clone results in the insertion of H-ras 5' sequences (-53 to +65) fused in frame 30 with the firefly luciferase gene. The resulting expression vector encodes a ras-luciferase fusion product which is expressed under control of the steroid-inducible MMTV promoter. These plasmid constructions contain sequences encoding amino acids 1-22 of activated (RA2) or normal (RA4) 35 H-ras proteins fused in frame with sequences coding for firefly luciferase. Translation initiation of the ras-luciferase fusion mRNA is dependent upon the natural H-ras

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is obtained and that this recognition results in stronger binding than DNA-RNA of the same sequences.

The thermal stability was measured as the melting temperature T_m , of complexes between PNA oligomers and their complementary ribonucleotide oligomers. Results were compared to phosphodiester ($P=O$) and phosphorothioate ($P=S$) oligomers complexed with complementary ribonucleotide oligomers. Results are shown in Table 3.

Table 3

SEQUENCE	SEQ ID NO:	PNA T_m °C	$P=S$ T_m °C	$P=O$ T_m °C
CTT ATA TTC CGT CAT CGC TC	2	76.5	48.8	58.1
TAT TCC GTC ATC GCT CCT CA	25	88.6	58.4	67.3

Absorbance vs. temperature curves were measured at 260 nm in 100mM NaCl, 10 mM Na-phosphate, 0.1 mM EDTA, pH 7. T_m , the temperature at which half of the molecules are hybridized was obtained by fitting triplicate melting curves at 4 μ M of each strand to a modified two state model with linear sloping baseline utilizing the procedure as published in Monia et al., *J. Biol. Chem.*, 1992, 267, 19954-19962.

20 Example 3

Ras-Luciferase Reporter Gene Assembly

The ras-luciferase reporter genes are assembled using PCR technology. Oligonucleotide primers are synthesized for use as primers for PCR cloning of the 5'-regions of exon 1 of both the mutant (codon 12) and non-mutant (wild-type) human H-ras genes. The plasmids pT24-C3, containing the c-H-ras1 activated oncogene (codon 12, GGC \rightarrow GTC), and pbc-N1, containing the c-H-ras proto-oncogene, are obtained from the American Type Culture Collection (Bethesda, MD). The plasmid pT3/T7 luc, containing the 1.9 kb firefly luciferase gene, is obtained from Clontech Laboratories (Palo Alto, CA). The oligonucleotide PCR primers are used in standard PCR reactions using mutant and non-mutant H-ras genes as templates. These primers produce a

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AUG codon. Both mutant and normal H-ras luciferase fusion constructions are confirmed by DNA sequence analysis using standard procedures.

Example 4

5 Transfection of Cells with Plasmid DNA Encoding H-ras

Transfections are performed as described by Greenberg, M.E., in *Current Protocols in Molecular Biology*, (F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.A. Smith, J.G. Seidman and K. Strahl, eds.), John Wiley and Sons, NY, with the following modifications. HeLa cells are plated on 60 mm dishes at 5×10^5 cells/dish. A total of 10 µg or 12 µg of DNA is added to each dish, of which 1 µg was a vector expressing the rat glucocorticoid receptor under control of the constitutive Rous sarcoma virus (RSV) promoter and the remainder is ras-luciferase reporter plasmid. Calcium phosphate-DNA coprecipitates are removed after 16-20 hours by washing with Tris-buffered saline [50 mM Tris-Cl (pH 7.5), 150 mM NaCl] containing 3 mM EGTA. Fresh medium supplemented with 10% fetal bovine serum is then added to the cells. At this time, cells are pre-treated with PNA oligomers prior to activation of reporter gene expression of dexamethasone. The PNA oligomers will be expected to be more stable than conventional antisense oligonucleotides with respect to degradation. The PNA oligomers also will be expected to be better membrane penetrators than conventional antisense oligonucleotides.

Example 5

PNA Oligomer Treatment of Cells Expressing H-ras

Following plasmid transfection, cells are washed with phosphate buffered saline (PBS) prewarmed to 37°C and Opti-MEM containing 5 µg/mL N-[1-(2,3-dioleyloxy)propyl]-N,N,N,-trimethylammonium chloride (DOTMA) is added to each plate (1.0 ml per well). PNA oligomers prepared in accordance with Example 1, having the following sequences:

35 CTTATATTCCGTCATCGCTC (SEQ ID NO: 2), TCCGTCATCGCTCCTCAGGG

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(SEQ ID NO: 3), TGCCCACACCGACGGCGCCACC (SEQ ID NO: 4), TTGCCCACACCGACGGCGCCACCA (SEQ ID NO: 5), GCCCACACCGACGGCGCCAC (SEQ ID NO: 9), CACACCGACGGCGCC (SEQ ID NO: 12), CCACACCGACGGCGCC (SEQ ID NO: 13),
5 CCCACACCGACGGCGCCA (SEQ ID NO: 14), CCACACCGACGGCGCC (SEQ ID NO: 21), CACACCGACGGCGCC (SEQ ID NO: 22), CCCACACCGACGGCGCC (SEQ ID NO: 23), CCACACCGACGGCGCCA (SEQ ID NO: 24) and TATTCCGTCATCGCTCCTCA (SEQ ID NO: 25), are added from 50 μ M stocks to each plate and incubated for 4 hours at 37°C.
10 Medium is removed and replaced with DMEM containing 10% fetal bovine serum and the appropriate PNA oligomer. The cells are incubated for an additional 2 hours at 37°C before reporter gene expression is activated by treatment with dexamethasone to a final concentration of 0.2 μ M. Cells are harvested and
15 assayed for luciferase activity, by techniques known in the art, fifteen hours following dexamethasone stimulation. Several PNA oligomers will be expected to give significant and reproducible inhibition of ras-luciferase activity. The observation that a PNA oligomer targeted to the ras
20 translation initiation codon is equally effective in reducing both mutant and normal ras expression is expected since the two targets have identical sequence compositions in the region surrounding the AUG translation initiation site. In addition, it is expected to observe PNA oligomers which
25 display selectivity toward the mutated form of ras-luciferase as compared to the normal form.

Example 6

PNA Oligomer Treatment of Cells Expressing K-ras in vitro

Human colon carcinoma cell lines Calu 1, SW480 and
30 SW620 are obtained from the American Type Culture Collection (ATCC) and cultured and maintained as monolayers on 6-well plates in Dulbecco's Modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum and 100 U/ml penicillin. Cells are treated with PNA oligomers prepared as
35 described in Example 1 and having sequences as set forth in Table 3 and K-ras mRNA expression is measured by Northern

- 35 -

blot analysis 24 hours later. For proliferation studies, cells are treated with a single dose of PNA oligomer at day zero and monitored over a five-day period.

Example 7

5 PNA Oligomer Treatment of Cells Expressing Mutant and Wild Type K-ras

SW480 cells and HeLa cells are cultured as in Example 6. Cells are treated with a single dose of PNA oligomers prepared as described in Example 1 and having 10 sequence as set forth in Table 3 and mRNA levels are determined by Northern blot analysis 24 hours later.

Example 8

Northern Blot Analysis of ras Expression in vivo

The human urinary bladder cancer cell line T24 is obtained from the American Type Culture Collection (Rockville MD). Cells are grown in McCoy's 5A medium with L-glutamine (Gibco BRL, Gaithersburg MD), supplemented with 10% heat-inactivated fetal calf serum and 50 U/ml each of penicillin and streptomycin. Cells are seeded on 100 mm plates. When they reach 70% confluence, they are treated with the aforementioned PNA oligomers directed to H-ras as described in Example 5. Plates are washed with 10 ml prewarmed PBS and 5 ml of Opti-MEM reduced-serum medium containing 2.5 μ l DOTMA. PNA oligomer is then added to the desired concentration. After 4 hours of treatment, the medium is replaced with McCoy's medium. Cells are harvested 48 hours after oligomer treatment and RNA is isolated using a standard CsCl purification method. Kingston, R.E., in *Current Protocols in Molecular Biology*, (F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.A. Smith, J.G. Seidman and K. Strahl, eds.), John Wiley and Sons, NY.

The human epithelioid carcinoma cell line HeLa 229 is obtained from the American Type Culture Collection (Bethesda, MD). HeLa cells are maintained as monolayers on 35 6-well plates in Dulbecco's Modified Eagle's medium (DMEM)

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supplemented with 10% fetal bovine serum and 100 U/ml penicillin. Treatment with the PNA oligomers directed to H-ras as described in Example 5 and isolation of RNA are essentially as described above for T24 cells.

5 Northern hybridization: 10 µg of each RNA is electrophoresed on a 1.2% agarose/formaldehyde gel and transferred overnight to GeneBind 45 nylon membrane (Pharmacia LKB, Piscataway, NJ) using standard methods. Kingston, R.E., in *Current Protocols in Molecular Biology*,
10 (F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.A. Smith, J.G. Seidman and K. Strahl, eds.), John Wiley and Sons, NY. RNA is UV-crosslinked to the membrane. Double-stranded ³²P-labeled probes are synthesized using the Prime a Gene labeling kit (Promega, Madison WI). The ras probe is a
15 SalI-NheI fragment of a cDNA clone of the activated (mutant) H-ras mRNA having a GGC-to-GTC mutation at codon-12. The control probe is G3PDH. Blots are prehybridized for 15 minutes at 68°C with the QuickHyb hybridization solution (Stratagene, La Jolla, CA). The heat-denatured radioactive
20 probe (2.5 x 10⁶ counts/2 ml hybridization solution) mixed with 100 µl of 10 mg/ml salmon sperm DNA is added and the membrane is hybridized for 1 hour at 68°C. The blots are washed twice for 15 minutes at room temperature in 2x SSC/0.1% SDS and once for 30 minutes at 60°C with
25 0.1XSSC/0.1%SDS. Blots are autoradiographed and the intensity of signal is quantitated using an ImageQuant PhosphorImager (Molecular Dynamics, Sunnyvale, CA). Northern blots are first hybridized with the ras probe, then stripped by boiling for 15 minutes in 0.1x SSC/0.1%SDS and
30 rehybridized with the control G3PDH probe to check for correct sample loading.

It is expected to observe the downregulation of ras mRNA as a result of treatment of cells with the PNA oligomers.

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Example 9

ras PNA Oligomer Inhibition of Proliferation of Cancer Cells

Cells are cultured and treated with the aforementioned PNA oligomers directed to ras essentially as described in Example 8. Cells are seeded on 60 mm plates and are treated with PNA oligomer in the presence of DOTMA when they reach 70% confluency. Time course experiment: On day 1, cells are treated with a single dose of PNA oligomer at a final concentration of 100 nM. The growth medium is changed once on day 3 and cells are counted every day for 5 days, using a counting chamber. Dose-response experiment: Various concentrations of PNA oligomer (10, 25, 50, 100 or 250 nM) are added to the cells and cells are harvested and counted 3 days later. It is expected to observe the reduction or abrogation of cancer cell proliferation as a result of treating the cells with PNA oligomers directed to ras.

Those skilled in the art will appreciate that numerous changes and modifications may be made to the preferred embodiments of the invention and that such changes and modifications may be made without departing from the spirit of the invention. It is therefore intended that the appended claims cover all such equivalent variations as fall within the true spirit and scope of the invention.

- 38 -

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Lima, Walter
Monia, Brett
Freier, Susan
Ecker, David

(ii) TITLE OF INVENTION: OLIGOMERS FOR MODULATING RAS ONCOGENE

(iii) NUMBER OF SEQUENCES: 39

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Woodcock Washburn Kurtz Mackiewicz and Norris
(B) STREET: One Liberty Place - 46th Floor
(C) CITY: Philadelphia
(D) STATE: PA
(E) COUNTRY: U.S.A.
(F) ZIP: 19103

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER:
(B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Gaumond, Rebecca R.
(B) REGISTRATION NUMBER: 35,152
(C) REFERENCE/DOCKET NUMBER:

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 215-568-3100
(B) TELEFAX: 215-568-3439

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 17
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

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 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
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 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
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 - (D) OTHER INFORMATION: /label = Modified-site /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- 40 -

- (ix) FEATURE:
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 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
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- 41 -

- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label= Modified-site
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Xaa
1 5 10 15

Xaa Xaa

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 20
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
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 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
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 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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- (B) LOCATION: 13
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- (ix) FEATURE:
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(B) LOCATION: 14
(D) OTHER INFORMATION: /label= Modified-site
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- (ix) FEATURE:
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- (ix) FEATURE:
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- (ix) FEATURE:
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(D) OTHER INFORMATION: /label= Modified-site
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- (ix) FEATURE:
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- (ix) FEATURE:
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(D) OTHER INFORMATION: /label= Modified-site
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- (ix) FEATURE:
(A) NAME/KEY: Modified-site
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(D) OTHER INFORMATION: /label= Modified-site
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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa
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(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
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N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

- 45 -

- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label= Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
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 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label= Modified-site
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- (ix) FEATURE:
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 - (B) LOCATION: 9
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- (ix) FEATURE:
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- (ix) FEATURE:
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/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site

- 46 -

- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label= Modified-site
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 - (B) LOCATION: 16
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- (ix) FEATURE:
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- (ix) FEATURE:
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/note = "Guanine heterocyclic base is attached to
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Xaa Xaa Xaa Xaa Xaa
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- 47 -

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

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- (B) LOCATION: 1
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N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site

- 48 -

/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label= Modified-site

- 49 -

/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 22
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /label= Modified-site

- 50 -

/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note= "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note= "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note= "Cytosine heterocyclic base is attached to

- 51 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to

- 52 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 18
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 19
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 20
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 21
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to

- 53 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 22
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 25
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Xaa
1 5 10 15

Xaa
20 25

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

- group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Xaa Xaa Xaa Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 7
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2

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(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 3
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 4
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 5
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 6
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 7
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Xaa Xaa Xaa Xaa Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site

- 58 -

/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site

- 59 -

/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /label = Modified-site

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/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 11
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
 /note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
 /note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
 /note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
 /note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
 /note= "Guanine heterocyclic base is attached to

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N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 13
- (B) TYPE: amino acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 1
(D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 2
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 3
(D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 4
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 5
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 6
(D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 7
(D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

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- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
 /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Xaa										
1	5		10							

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 15
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Xaa
1 5 10 15

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(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site

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/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label= Modified-site

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/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Xaa
1 5 10 15

Xaa Xaa

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

- group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

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- group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 12
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 13
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 14
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 15
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 16
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 17
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 18
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 19
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

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group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Adenine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Xaa	Xaa	Xaa	Xaa
1	5	10	

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
 /note = "Guanine heterocyclic base is attached to

- 73 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to

- 74 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Uracil heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Uracil heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

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- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Uracil heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Uracil heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Uracil heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10

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- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Xaa
1 5 10

(2) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to

- 81 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to

- 82 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Xaa
1 5 10 15

Xaa

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site /note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Xaa
1 5 10 15

Xaa

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6

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- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 7
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 8
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 9
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 10
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 11
(D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 12
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 13
(D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 14

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(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 15
(D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 16
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 17
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 18
(D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Xaa
1 5 10 15

Xaa Xaa Xaa

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 1
(D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Cytosine heterocyclic base is attached to

- 88 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to

- 89 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to

- 90 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Xaa
1 5 10 15

Xaa Xaa Xaa

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 18
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 19
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 20
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Xaa
1 5 10 15
Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

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- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site



WO 94/28720

PCT/US94/06620

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- (B) LOCATION: 14
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 15
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 16
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 17
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 18
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 19
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."
- (ix) FEATURE:
 (A) NAME/KEY: Modified-site
 (B) LOCATION: 20
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Xaa											
1	5	10	15								

Xaa	Xaa	Xaa	Xaa
20			

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SANTARIS

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
 /note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Xaa											
1	5	10									15

Xaa	Xaa
Xaa	Xaa
	20

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Xaa											
1	5		10		15						

Xaa										
					20					

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

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- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site

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- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site

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- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
1	5		10			15					
Xaa Xaa Xaa Xaa Xaa											
20											

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE

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/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label= Modified-site

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/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

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- group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 5
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 6
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 7
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 8
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 9
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 10
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 11
(D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 12
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl

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group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

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group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6

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- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 14

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(D) OTHER INFORMATION: /label = Modified-site
 /note = "Thymine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 15

(D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 16

(D) OTHER INFORMATION: /label = Modified-site
 /note = "Cytosine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 17

(D) OTHER INFORMATION: /label = Modified-site
 /note = "Adenine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Xaa										
1	5		10			15				

Xaa	Xaa
17	

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 1
 (D) OTHER INFORMATION: /label = MODIFIED-SITE
 /note = "Guanine heterocyclic base is attached to
 N-acetyl(2-aminoethyl)glycine through the N-acetyl
 group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 2
 (D) OTHER INFORMATION: /label = Modified-site
 /note = "Thymine heterocyclic base is attached to

- 116 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to

- 117 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to

- 118 -

N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Xaa											
1	5		10		15						

Xaa											
			20								

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 11
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 18
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

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- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 5
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 6
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 7
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 8
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 9
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 10
 - (D) OTHER INFORMATION: /label = Modified-site
/note= "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site

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- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 12
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 13
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 15
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 16
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 17
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 18
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site

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- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:37:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 1
 - (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 2
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 3
 - (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 4
 - (D) OTHER INFORMATION: /label = Modified-site

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/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site

- 126 -

/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 13

(D) OTHER INFORMATION: /label = Modified-site

/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 14

(D) OTHER INFORMATION: /label = Modified-site

/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 15

(D) OTHER INFORMATION: /label = Modified-site

/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 16

(D) OTHER INFORMATION: /label = Modified-site

/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 17

(D) OTHER INFORMATION: /label = Modified-site

/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 18

(D) OTHER INFORMATION: /label = Modified-site

/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 19

(D) OTHER INFORMATION: /label = Modified-site

/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 20

(D) OTHER INFORMATION: /label = Modified-site

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/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa
20

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 15
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl*

- 128 -

- group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 6
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 7
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 8
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 9
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 10
(D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 11
(D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 12
(D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 13
(D) OTHER INFORMATION: /label = Modified-site
/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl

- 129 -

group."

- (ix) FEATURE:
- (A) NAME/KEY: Modified-site
 - (B) LOCATION: 14
 - (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Xaa
1 5 10 15

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /label= MODIFIED-SITE
/note= "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 2
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /label= Modified-site
/note= "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /label= Modified-site

- 130 -

/note = "Thymine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 8
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Cytosine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Adenine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /label = Modified-site
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /label = MODIFIED-SITE
/note = "Guanine heterocyclic base is attached to N-acetyl(2-aminoethyl)glycine through the N-acetyl group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 13
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 14
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Thymine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /label = Modified-site
*/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."*

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /label = Modified-site

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/note = "Cytosine heterocyclic base is attached to
N-acetyl(2-aminoethyl)glycine through the N-acetyl
group."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Xaa
1 5 10 15
Xaa Xaa Xaa Xaa Xaa
20

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WHAT IS CLAIMED IS:

1. An oligomer comprising at least one peptide nucleic acid subunit and having a sequence selected from the group consisting of:

CCACACCGCCGGCGCCC (SEQ ID NO: 1);
CTTATATTCCGTATCGCTC (SEQ ID NO: 2);
TCCGTCATCGCTCCTCAGGG (SEQ ID NO: 3);
TGCCCCACACCGACGGCGCCCACC (SEQ ID NO: 4);
TTGCCAACACCGACGGCGCCCACCA (SEQ ID NO: 5);
CGACG (SEQ ID NO: 6);
CCGACGG (SEQ ID NO: 7);
ACCGACGGC (SEQ ID NO: 8);
GCCACACCGACGGCGCCCAC (SEQ ID NO: 9);
CACCGACGGCG (SEQ ID NO: 10);
ACACCGACGGCGC (SEQ ID NO: 11);
CACACCGACGGCGCC (SEQ ID NO: 12);
CCACACCGACGGCGCCC (SEQ ID NO: 13);
CCCACACCGACGGCGCCCA (SEQ ID NO: 14);
CACCAACCACC (SEQ ID NO: 15);
GCGCCCACCA (SEQ ID NO: 16);
UUGCCCACAC (SEQ ID NO: 17);
CACUCUUGCC (SEQ ID NO: 18);
CACACCGACCG (SEQ ID NO: 19);
CGACGGCGCC (SEQ ID NO: 20);
CCACACCGACGGCGCC (SEQ ID NO: 21);
CACACCGACGGCGCCC (SEQ ID NO: 22);
CCCACACCGACGGCGCCC (SEQ ID NO: 23);
CCACACCGACGGCGCCCA (SEQ ID NO: 24);
TATTCCGTATCGCTCCTCA (SEQ ID NO: 25);
CTGCCTCCGCCGCCGCGGCC (SEQ ID NO: 26);
CAGTGCCTGCGCCGCCCTCG (SEQ ID NO: 27);
AGGCCTCTCTCCCGCACCTG (SEQ ID NO: 28);
TTCAGTCATTTCAGCAGGC (SEQ ID NO: 29);
TTATATTCAAGTCATTTCAAG (SEQ ID NO: 30);
CAAAGTTTATATTCAAGTCATT (SEQ ID NO: 31);
GCCTACGCCACCAAGCTCCAAC (SEQ ID NO: 32);
CTACGCCACCAAGCTCCA (SEQ ID NO: 33);

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GTACTCCTCTTGACCTGCTGT (SEQ ID NO: 34);
CCTGTAGGAATCCTCTATTGT (SEQ ID NO: 35);
GGTAATGCTAAAACAAATGC (SEQ ID NO: 36);
GGAATACTGGCACTTCGAGG (SEQ ID NO: 37);
TACGCCAACAGCTCC (SEQ ID NO: 38); and
TTTCAGCAGGCCTCTCTCC (SEQ ID NO: 39).

2. The oligomer of claim 1 wherein the sequence of the oligomer is selected from the group consisting of:

CTTATATTCCGTCATCGCTC (SEQ ID NO: 2);
TCCGTCATCGCTCCTCAGGG (SEQ ID NO: 3);
TGCCCACACCGACGGCGCCCACC (SEQ ID NO: 4);
TTGCCCACACCGACGGCGCCCACCA (SEQ ID NO: 5);
GCCCACACCGACGGCGCCCAC (SEQ ID NO: 9);
CACACCGACGGCGCC (SEQ ID NO: 12);
CCACACCGACGGCGCCC (SEQ ID NO: 13);
CCCACACCGACGGCGCCC (SEQ ID NO: 14);
CCACACCGACGGCGCC (SEQ ID NO: 21);
CACACCGACGGCGCCC (SEQ ID NO: 22);
CCCACACCGACGGCGCCC (SEQ ID NO: 23);
CCACACCGACGGCGCCC (SEQ ID NO: 24);
TATTCCGTCATCGCTCCTCA (SEQ ID NO: 25);
CTGCCCTCCGCCGCCGCC (SEQ ID NO: 26);
CAGTGCCTGCGCCGCGCTCG (SEQ ID NO: 27);
AGGCCTCTCTCCCGCACCTG (SEQ ID NO: 28);
TTCAGTCATTTCAGCAGGC (SEQ ID NO: 29);
TTATATTCAAGTCATTTCAAG (SEQ ID NO: 30);
CAAGTTTATATTCAAGTCATT (SEQ ID NO: 31);
GCCTACGCCACCAAGCTCCAAC (SEQ ID NO: 32);
CTACGCCACCAAGCTCCA (SEQ ID NO: 33);
GTACTCCTCTTGACCTGCTGT (SEQ ID NO: 34);
CCTGTAGGAATCCTCTATTGT (SEQ ID NO: 35);
GGTAATGCTAAAACAAATGC (SEQ ID NO: 36);
GGAATACTGGCACTTCGAGG (SEQ ID NO: 37);
TACGCCAACAGCTCC (SEQ ID NO: 38); and
TTTCAGCAGGCCTCTCTCC (SEQ ID NO: 39).

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3. The oligomer of claim 1 wherein substantially all the subunits of the oligomer are peptide nucleic acid subunits.

4. The oligomer of claim 1 incorporated in a pharmaceutically acceptable carrier.

5. An oligomer hybridizable to AUG region, 3' untranslated region, or codon 12 region of H-ras and comprising at least one peptide nucleic acid subunit.

6. An oligomer hybridizable to AUG region, 3' untranslated region, 5' untranslated region, codon 12, codon 38 or codon 61 of K-ras comprising at least one peptide nucleic acid subunit.

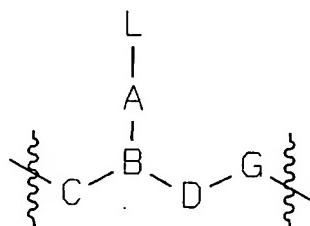
7. An oligomer having a sequence selected from the group consisting of:

CCACACCGCCGGCGCCC (SEQ ID NO: 1);
CTTATATTCCGTCATCGCTC (SEQ ID NO: 2);
TCCGTCATCGCTCCTCAGGG (SEQ ID NO: 3);
TGCCCCACACCGACGGCGCCACC (SEQ ID NO: 4);
TTGCCCCACACCGACGGCGCCCACCA (SEQ ID NO: 5);
CGACG (SEQ ID NO: 6);
CCGACGG (SEQ ID NO: 7);
ACCGACGGC (SEQ ID NO: 8);
GCCAACACCGACGGCGCCAC (SEQ ID NO: 9);
CACCGACGGCG (SEQ ID NO: 10);
ACACCGACGGCGC (SEQ ID NO: 11);
CACACCGACGGCGCC (SEQ ID NO: 12);
CCACACCGACGGCGCCC (SEQ ID NO: 13);
CCCACACCGACGGCGCCCA (SEQ ID NO: 14);
CACCAACCACC (SEQ ID NO: 15);
GCGCCCCACCA (SEQ ID NO: 16);
UUGCCCCACAC (SEQ ID NO: 17);
CACUCUUGCC (SEQ ID NO: 18);
CACACCGACG (SEQ ID NO: 19);

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CGACGGCGCC (SEQ ID NO: 20);
 CCACACCGACGGCGCC (SEQ ID NO: 21);
 CACACCGACGGCGCCC (SEQ ID NO: 22);
 CCCACACCGACGGCGCCC (SEQ ID NO: 23);
 CCACACCGACGGCGCCA (SEQ ID NO: 24);
 TATTCCGTCATCGCTCCTCA (SEQ ID NO: 25);
 CTGCCTCCGCCGCCGCC (SEQ ID NO: 26);
 CAGTGCCTGCGCCGCCGCTCG (SEQ ID NO: 27);
 AGGCCTCTCTCCGCACCTG (SEQ ID NO: 28);
 TTCAGTCATTTCAGCAGGC (SEQ ID NO: 29);
 TTATATTCAGTCATTTCAG (SEQ ID NO: 30);
 CAAGTTTATATTAGTCATT (SEQ ID NO: 31);
 GCCTACGCCACCAGCTCCAAC (SEQ ID NO: 32);
 CTACGCCACCAGCTCCA (SEQ ID NO: 33);
 GTACTCCTCTTGACCTGCTGT (SEQ ID NO: 34);
 CCTGTAGGAATCCTCTATTGT (SEQ ID NO: 35);
 GGTAATGCTAAAACAAATGC (SEQ ID NO: 36);
 GGAATACTGGCACTTCGAGG (SEQ ID NO: 37);
 TACGCCAACAGCTCC (SEQ ID NO: 38); and
 TTTTCAGCAGGCCTCTCTCC (SEQ ID NO: 39).

wherein at least one subunit of the oligomer has the formula:



(I)

wherein:

L is one of the adenine, thymine, cytosine or guanine heterocyclic bases of the oligomer;

C is (CR^6R^7) , where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are independently selected from the group consisting of hydrogen, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, NR^3R^4 and SR^5 , where each of R^3 and R^4 is

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independently selected from the group consisting of hydrogen, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio and amino; and R^5 is hydrogen, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

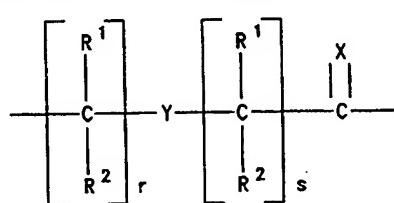
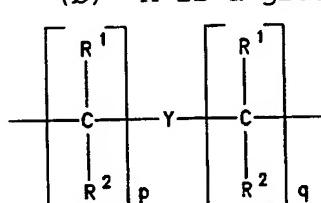
D is $(CR^6R^7)_z$, where R^6 and R^7 are as defined above; each of y and z is zero or an integer from 1 to 10, the sum $y + z$ being greater than 2 but not more than 10;

G is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

each pair of A and B is selected such that:

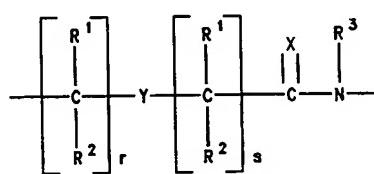
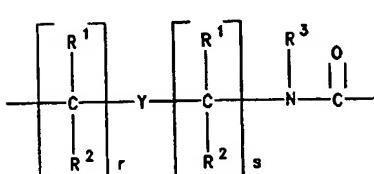
(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+ ; or

(b) A is a group of formula (IId) and B is CH;



(IIa)

(IIb)



(IIc)

(IId)

where:

X is O, S, Se, NR^3 , CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4 ;

each of p and q is zero or an integer from 1 to 5, the sum $p+q$ being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum $r+s$ being not more than 10; and

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each R¹ and R² is independently selected from the group consisting of hydrogen, (C₁-C₄)alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen.

8. The oligomer of claim 7 wherein A is CH₂CO, B is N, C is CH₂ and D is CH₂.

9. The oligomer of claim 7 wherein all of the subunits are peptide nucleic acid subunits;

said oligomer including a group Q on one end of said oligomer and a group I on the other end of said oligomer;

Q is -CO₂H, -CONR'R'', -SO₃H or -SO₂NR'R'' or an activated derivative of -CO₂H or -SO₃H; and

I is -NHR'''R'''' or -NR'''C(O)R'''', where R', R'', R''' and R'''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

10. A method of modulating the expression of a human ras gene comprising contacting tissues or cells containing the gene with an oligomer comprising a sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 39 and having at least one peptide nucleic acid subunit.

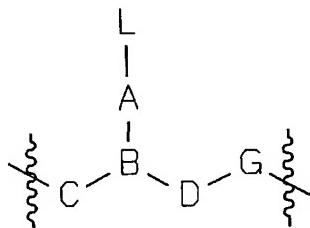
11. The method of claim 10 wherein the human ras gene is H-ras and the sequence is selected from the group consisting of SEQ ID NO:1 through SEQ ID NO: 25.

12. The method of claim 10 wherein the human ras gene is K-ras and the sequence is selected from the group consisting of SEQ ID NO: 26 through SEQ ID NO: 39.

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13. The method of claim 10 wherein substantially all of the subunits of the oligomer are peptide nucleic acid subunits.

14. A method of modulating the expression of a human ras gene comprising contacting tissues or cells containing the gene with an oligomer comprising a sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 39 wherein at least one subunit of the oligomer has the formula:



(I)

wherein:

L is one of the adenine, thymine, cytosine or guanine heterocyclic bases of the oligomer;

C is $(CR^6R^7)_y$, where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are independently selected from the group consisting of hydrogen, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, NR^3R^4 and SR^5 , where each of R^3 and R^4 is independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio and amino; and R^5 is hydrogen, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6) alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

D is $(CR^6R^7)_z$, where R^6 and R^7 are as defined above; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

- 140 -

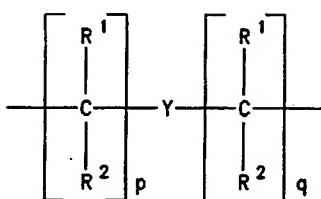
G is $-\text{NR}^3\text{CO}-$, $-\text{NR}^3\text{CS}-$, $-\text{NR}^3\text{SO}-$ or $-\text{NR}^3\text{SO}_2-$, in either orientation, where R^3 is as defined above;

each pair of A and B is selected such that:

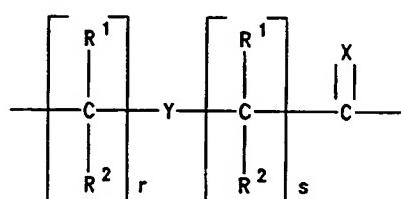
(a) A is a group of formula (IIa), (IIb) or (IIc)

and B is N or R^3N^+ ; or

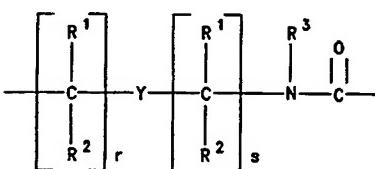
(b) A is a group of formula (IId) and B is CH;



(IIa)

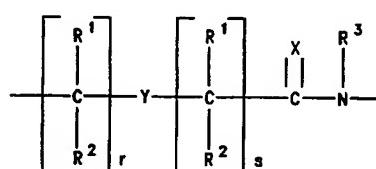


(IIb)



(IIc)

where:



(IId)

X is O, S, Se, NR^3 , CH_2 or $\text{C}(\text{CH}_3)_2$;

Y is a single bond, O, S or NR^4 ;

each of p and q is zero or an integer from 1 to 5, the sum p+q being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum r+s being not more than 10; and

each R^1 and R^2 is independently selected from the group consisting of hydrogen, $(\text{C}_1\text{-}\text{C}_4)\text{alkyl}$ which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen.

15. The method of claim 14 wherein A is CH_2CO , B is N, C is CH_2 and D is CH_2 .

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16. The method of claim 14 wherein all of the subunits are peptide nucleic acid subunits; said oligomer including a group Q on one end of said oligomer and a group I on the other end of said oligomer;
Q is -CO₂H, -CONR'R'', -SO₃H or -SO₂NR'R'' or an activated derivative of -CO₂H or -SO₃H; and
I is -NHR'''R'''' or -NR'''C(O)R''''', where R', R'', R''' and R''''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

17. The method of claim 14 wherein the human ras gene is H-ras and the sequence is selected from the group consisting of SEQ ID NO:1 through SEQ ID NO: 25.

18. The method of claim 14 wherein the human ras gene is K-ras and the sequence is selected from the group consisting of SEQ ID NO: 26 through SEQ ID NO: 39.

19. A method of treating conditions arising from the activation of a ras oncogene comprising contacting an animal with an oligomer comprising a sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 39 and having at least one peptide nucleic acid subunit.

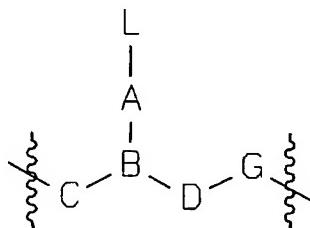
20. The method of claim 19 wherein the ras oncogene is H-ras and the sequence is selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 25.

21. The method of claim 19 wherein the ras oncogene is K-ras and the sequence is selected from the group consisting of SEQ ID NO: 26 through SEQ ID NO: 39.

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22. The method of claim 19 wherein substantially all of the subunits of the oligomer are peptide nucleic acid subunits.

23. A method of treating conditions arising from the activation of a ras oncogene comprising contacting an animal with an oligomer comprising a sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 39 wherein at least one subunit of the oligomer has the formula:



(I)

wherein:

L is one of the adenine, thymine, cytosine or guanine heterocyclic bases of the oligomer;

C is $(CR^6R^7)_y$, where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are independently selected from the group consisting of hydrogen, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, NR^3R^4 and SR^5 , where each of R^3 and R^4 is independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio and amino; and R^5 is hydrogen, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6) alkyl, or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

D is $(CR^6R^7)_z$ where R^6 and R^7 are as defined above; each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

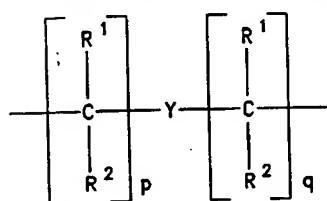
G is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

each pair of A and B is selected such that:

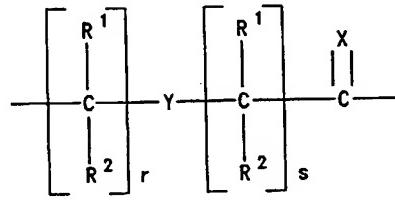
- 143 -

(a) A is a group of formula (IIa), (IIb) or (IIc)
and B is N or R^3N^+ ; or

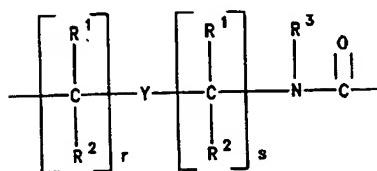
(b) A is a group of formula (IId) and B is CH;



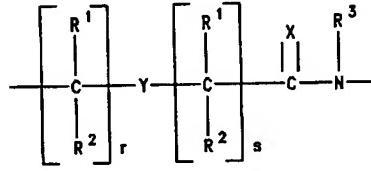
(IIa)



(IIb)



(IIc)



(IId)

where:

X is O, S, Se, NR^3 , CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4 ;

each of p and q is zero or an integer from 1 to 5, the sum p+q being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum r+s being not more than 10; and

each R^1 and R^2 is independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen.

24. The method of claim 23 wherein A is CH_2CO , B is N, C is CH_2 and D is CH_2 .

25. The method of claim 23 wherein all of the subunits are peptide nucleic acid subunits;

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said oligomer including a group Q on one end of said oligomer and a group I on the other end of said oligomer;

Q is -CO₂H, -CONR'R'', -SO₃H or -SO₂NR'R'' or an activated derivative of -CO₂H or -SO₃H; and

I is -NHR'''R'''' or -NR'''C(O)R''''', where R', R'', R''' and R''''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

26. The method of claim 23 wherein the ras oncogene is H-ras and the sequence is selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 25.

27. The method of claim 23 wherein the ras oncogene is K-ras and the sequence is selected from the group consisting of SEQ ID NO: 26 through SEQ ID NO: 39.

28. A method of detecting the presence of a ras gene in cells or tissues comprising contacting the cells or tissues with an oligomer comprising a sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 39 and having at least one peptide nucleic acid subunit.

29. The method of claim 28 wherein the ras oncogene is H-ras and the sequence is selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 25.

30. The method of claim 28 wherein the ras oncogene is K-ras and the sequence is selected from the group consisting of SEQ ID NO: 26 through SEQ ID NO: 39.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/06620

A. CLASSIFICATION OF SUBJECT MATTER

IPC(S) : A01N 43/04; A61K 31/70, 37/00; C07H 17/00; C12N 15/00
 US CL : 435/172.3; 514/2, 44; 530/300; 536/24.1, 24.3

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/172.3; 514/2, 44; 530/300; 536/24.1, 24.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, DIALOG

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 92/20702 (BUCHARDT ET AL) 26 NOVEMBER 1992, see entire document.	1-30
Y	US. A, 4,871,838 (BOS ET AL) 03 OCTOBER 1989, see entire document.	1-30
Y	US. A, 5,087,617 (SMITH) 11 February 1992, see entire document.	1-30
Y	Anti-Cancer Drug Design, Volume 4, issued March 1989, Chang et al, "Comparative Inhibition of ras p21 Protein Synthesis with Phosphorus-Modified Antisense Oligonucleotides", pages 221-232, see entire document.	1-30

Further documents are listed in the continuation of Box C.

See patent family annex.

-	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reasons (as specified)	"Z"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
04 AUGUST 1994

Date of mailing of the international search report
19 AUG 1994

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Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/06620

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Science, Volume 254, issued 06 December 1991, Nielsen et al, "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", pages 1497-1500, see entire document.	1-30
Y,A	Chemical Reviews, Volume 90, Number 4, issued June 1990, Uhlmann et al, "Antisense Oligonucleotides: A New Therapeutic Principle", pages 543-584, see entire document.	1-30
A	Angewandte Chemie, Volume 31, Number 4, issued August 1992, Meier et al, "Peptide Nucleic Acids (PNAs)-Unusual Properties of Nonionic Oligonucleotide Analogues", pages 1008-1010, see entire document.	1-30